

Original Article

Natural History of Wolff–Parkinson–White Syndrome Detected via School-Based Electrocardiography Screening

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Background: Studies have indicated varying prevalence rates of Wolff–Parkinson–White (WPW) syndrome in young people, with various ages at initial episode of tachycardia. We aimed to investigate the incidence of subsequent tachycardia in asymptomatic schoolchildren who are first diagnosed as having WPW syndrome via secondary screening at our hospital.

Methods: From April 2011 to December 2023, 82 patients with suspected WPW syndrome based on school-based electrocardiograms (ECGs) underwent the second cardiac screening at our department. Of these, 62 patients (37 male patients) were diagnosed with WPW syndrome. Whether tachycardia occurred or not, age at onset if occurred, and ECG features were analyzed.

Results: Tachycardia occurred in 11 (18%) of the 62 patients, not significantly differing between sexes. Age at onset of tachycardia ranged from 10 to 16 years old, with the highest frequency observed at 12 years old (36%). Tachycardia was most frequently observed in patients with type A WPW syndrome (positive delta wave in lead V1); whereas the type of WPW syndrome did not differ between the tachycardia and the non-tachycardia groups. Additionally, no tachycardic episodes were observed in the 11 patients with intermittent WPW syndrome. The delta-wave amplitude seemed higher in the tachycardia group versus the non-tachycardia group, but this result was not statistically significant.

Conclusion: In the clinical follow-up of asymptomatic patients with WPW syndrome, when tachycardia attacks tend to occur should be taken into account to avoid delay in appropriate therapeutic intervention.

Keywords: Wolff–Parkinson–White syndrome, tachycardia, school, electrocardiography

Introduction

In Japan, Wolff–Parkinson–White (WPW) syndrome is detected in approximately 0.1% of all school electrocardiogram (ECG) examinations, with the latest statistics showing a rate of 0.082% across all grades.¹⁾ School ECG screening has been compulsory since 1995; children undergo ECG in their first year of primary school, junior high school, and high school. In some municipalities, additional screening is also to be performed in other grades. ECG screening is based on ECG-interpretation

guidelines, and children with certain features that are extracted, including those with WPW syndrome, are instructed to visit medical institutions.²⁾

A certain number of schoolchildren with WPW syndrome are detected by such screening and they are eligible for follow-up. Accurate information on the risk of tachycardia should be provided for these asymptomatic patients, leading to early therapeutic intervention such as electrophysiological study (EPS). In this study, we aimed to investigate the natural history of patients with WPW syndrome detected via school ECG screen-

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ing in our department, paying attention to age when attack of tachycardia first occurs and associated risk factors.

Materials and Methods

From April 2011 to December 2023, 82 patients with suspected WPW syndrome upon school ECG screening visited our department for the second screening. In these patients, the ECG was visually re-evaluated according to interpretation guidelines, and 20 patients were excluded because they did not meet diagnostic criteria such as a PR interval < 0.12 s and presence of a clear delta wave. The remaining 62 patients were definitively diagnosed with WPW syndrome, and included in the study. For these patients, we confirmed their history of tachycardia symptoms according to the initial interview. No patients had been diagnosed with WPW syndrome before the school ECG examination. No patients with structural abnormalities in the heart upon echocardiography or complications from other systemic diseases were included in this study. The study was approved by the hospital's Ethics Committee.

Tachycardia was defined as a palpitating attack with a definite onset and cessation, clearly recognized by the patient as abnormal, and confirmed via a careful interview. Patients with tachycardia attack were placed under careful observation and were indicated for medication and an EPS. Patients' age at their first tachycardia attack and sex-related differences were also examined. Based on the most common atrioventricular accessory pathway (AVAP) location observed on the ECG, we classified patients into types A (positive delta wave in lead V1: left-sided AVAP), type B ("rS pattern" in lead V1: right-sided AVAP), and type C ("QS pattern" in lead V1: septal AVAP), and comparing the frequency of tachycardia attacks among these types.^{3, 4)} Also investigated were differences in terms of persistent WPW syndrome (delta waves always present) and intermittent WPW syndrome (delta waves appearing intermittently). The latter was diagnosed when one or more ECGs, either at rest or for the Master two-step test, exhibited the intermittent appearance of delta waves.

The PR interval and QRS width were automatically measured and visually confirmed on ECG (ECG data-management system: EFS-8800; Fukuda Denshi, Tokyo). The delta-wave amplitude (DWA; in mm) was also measured retrospectively. It is considered useful for

differentiating of fasciculo-ventricular pathways (FVPs) from the AVAP of WPW syndrome.

The DWA was defined as the maximum height of the delta waves in the first 40ms of the most pre-excited frontal limb-lead QRS complex, according to previous reports.^{5, 6)} The DWA was measured manually on an ECG viewer by a single, blinded author and compared between the tachycardia and the non-tachycardia groups. One additional author measured the DWA on all ECGs via the same method to assess intra-rater reliability.

Statistical Analysis

All statistical analyses were performed using EZR (Jichi Medical University Saitama Medical Center, Saitama, Japan), a software package that extends the capabilities of R and R Commander.⁷⁾ Fisher's exact test was used to compare the seizure incidence between patients with persistent WPW syndrome and those with intermittent WPW syndrome and between the sexes. Kaplan–Meier curves were constructed to compare tachycardia attacks among patients with ECG types A, B, and C, and log-rank tests were used to evaluate those differences for statistical significance. The Mann–Whitney *U* test was used to compare the PR interval, QRS width, and DWA between the tachycardia and the non-tachycardia groups. Spearman's rank correlation coefficient was used to assess inter-observer variability. The normality of distributions was assessed using the Shapiro–Wilk normality test. A *p*-value < 0.05 was considered statistically significant.

Results

Among the 62 patients with a confirmed diagnosis of WPW syndrome, 37 (59.7%) were male. Age at diagnosis ranged from 6 to 16 years, and a median age at diagnosis was 10.5 (interquartile range: 6–13) years. The maximum follow-up period was 12 years, with a median of 4 (interquartile range: 2–6) years. In two cases, a history of tachycardia had been established at the time of the first visit. Based on the ECG features, 26 (41.9%) patients had type A, 16 (25.8%) had type B, and 20 (32.3%) had type C AVAP. Eleven patients (17.7%) had intermittent WPW syndrome.

Tachycardic attack occurred in 11 (17.7%) of the 62 patients during follow-up, and the incidence of tachycardia did not differ significantly between the sexes

($p=0.101$; Table 1). Age at tachycardia onset ranged from 10 to 16 years old; for the largest number of patients ($n=4$, 36.4%), tachycardia onset occurred at the age of 12 years old (Fig. 1). Tachycardia occurred in seven patients with type A, two with type B, and two with type C AVAP (Table 1). Type A was the most prevalent; still, the three groups did not differ in terms of tachycardic attacks ($p=0.463$; Fig. 2). Tachycardia was not observed in the intermittent WPW syndrome group, although the difference in syndrome types did not differ statistically between patients with and without tachycardia ($p=0.188$; Table 1).

PR interval, QRS width, and DWA did not differ between the tachycardia and the non-tachycardia groups ($p=0.963$, $p=0.778$, and $p=0.074$, respectively; Fig. 3). The Spearman rank correlation coefficient for inter-rater reliability of the two authors for DWA measurement was 0.588 ($p<0.001$).

None of the 11 patients who experienced tachycardia had an ECG record of the attack.

EPS and catheter ablation was performed in six of them. Of the five patients who have not undergone EPS, one patient is awaiting it, and three patients receive antiarrhythmic drugs. The remaining one is to be fol-

lowed up without medication at the patient's request. No sudden deaths or near misses were observed in this study.

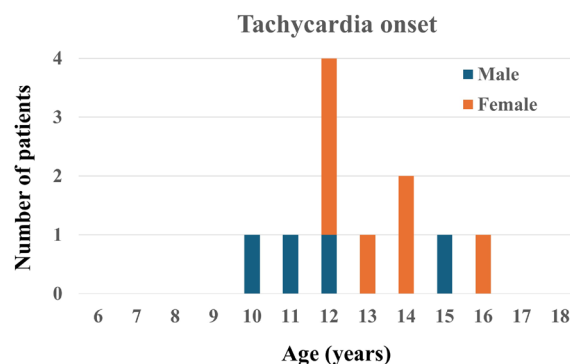


Fig. 1 Number of patients by age at onset of supra-ventricular tachycardic attacks

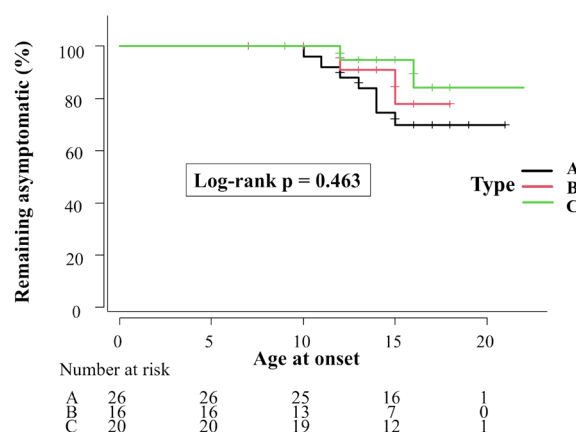


Fig. 2 Event-free survival curves of the onset of tachycardia in terms of ECG types A, B, and C ECG, electrocardiogram

Table 1 Comparison based on presence or absence of tachycardia

	Tachycardia (+)	Tachycardia (-)	
Total, n (%)	11 (17.7)	51 (82.3)	
Male, n (%)	4 (36.3)	33 (64.7)	$p=0.101$
ECG type A/B/C	7/2/2	19/14/18	
Intermittent type	0	11	$p=0.188$

ECG, electrocardiogram

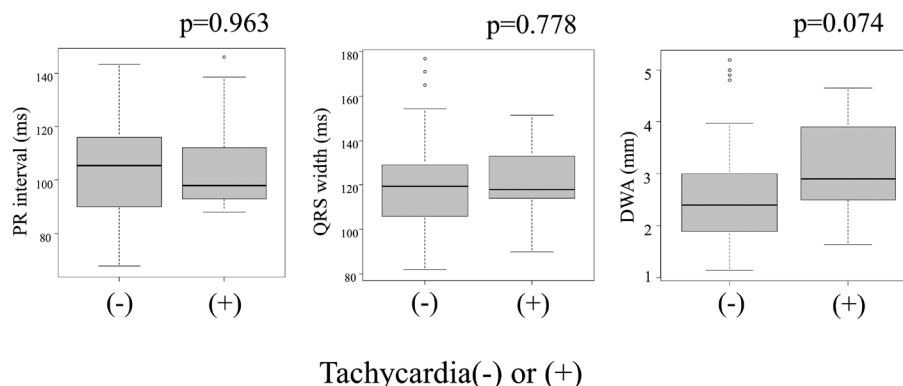


Fig. 3 Distribution and comparison of the PR interval (ms), QRS width (ms), and DWA (mm) in the tachycardia and the non-tachycardia groups DWA, delta-wave amplitude

Discussion

According to sources outside Japan, the prevalence of WPW syndrome is approximately 1 in 1,000 people.^{8–15)} The proportion of male individuals in the large studies ranged from 61.0% to 68.7%, almost twice that of female individuals.^{8–13)} Our survey revealed a similar trend, with 59.7% of patients being male.

The incidence of supraventricular tachycardia in WPW syndrome varies considerably according to study cohorts. Cain et al. in 2013 reported an incidence of 54%; obviously, they included patients with congenital heart defects, such as Ebstein's anomaly.¹⁵⁾ Other reports based on ECG screening, such as screening at school, revealed incidences of supraventricular tachycardia of approximately 10–20%.^{10–13)} In a previous study on schoolchildren in Japan, the incidence of tachycardia among students with WPW syndrome was 16%.¹²⁾ Similarly, in our study, the incidence of tachycardia in schoolchildren with WPW syndrome was 18%. None of the patients with intermittent WPW syndrome experienced tachycardic attacks. Although the risk of tachycardia is generally considered low in such patients, reports during the last 15 years suggested that this was not always the case.^{16, 17)} Type A WPW appeared more common among the tachycardia group; however, the prevalence of the types did not significantly correlate with tachycardia. Therefore, clinicians should be equally cautious for all three types.

In 1990, Perry and Garson reported two peaks in the age of onset of supraventricular tachycardia in the natural history of WPW syndrome; infancy (<1 year old) and 6–8 years old. They also discovered the third and less prominent peak at approximately 13 years of age.¹⁸⁾ This smaller peak is consistent with the peak observed in our series of patients with asymptomatic WPW syndrome detected via ECG screening, at the age of 12 years. The common finding of tachycardia around puberty suggests that several factors specific to this age group as well as physical growth may contribute to its development of tachycardia. Puberty hormones, including estrogen, thyroid hormones, growth hormones, insulin, and insulin-like growth factor 1 contribute to increased vasodilation and altered adrenergic sensitivity. Physical symptoms reflecting autonomic nervous system (ANS) dysfunction, such as vasovagal syncope and postural orthostatic tachycardia syndrome (POTS), are known to increase with the

onset of puberty. Changes in the ANS during this phase of life can also affect the refractory period of atrioventricular conduction, which forms part of the reentry circuit.^{19–21)}

We further examined the relationship between DWA and the occurrence of tachycardia, which has been reported as useful for the extraction of FVPs.²²⁾ In patients with WPW syndrome, those with certain FVPs are not at risk for tachycardia or sudden cardiac death, and thus they do not require attention. Approximately 1–5% of patients referred for EPS owing to preexcitation reportedly have FVPs.²³⁾ O'Leary et al. reported the validity of the DWA in differentiating AVAPs from FVPs. They compared the characteristics of body-surface ECGs between patients diagnosed with FVPs and those WPW syndrome with anterior septal accessory conduction pathways, reporting that a DWA >5 mm had a 96% specificity for AVAPs and a DWA <2 mm had a 96% specificity for FVPs. They suggested that an adenosine stress test would better be performed for differential diagnosis of asymptomatic patients with WPW-type ECGs and a DWA of 2–5 mm.²²⁾ The examination of the DWA in this study revealed no significant difference between patients with tachycardia and those without. Although FVPs were estimated to be prevalent in the non-tachycardia group, the DWA was not a significant predictor of tachycardia. Furthermore, although the inter-rater agreement was significant between two of the authors, the level of agreement was not satisfactory. This fact raises concerns about inter-rater variability in manual measurements.

WPW syndrome is an important finding in ECG screening at school, often resulting in early diagnosis and management. For reference, we also present the proportion of diseases diagnosed in schoolchildren who underwent such a screening and visited our hospital for management from 2012 to 2020 (Fig. 4). Of the 1,754 patients who visited the department, 346 (19.7%) patients required management. Among those 346, WPW syndrome was the second most frequent diagnosis after premature ventricular contraction in key grades, comprising 20% in the first year of elementary school, 16% in the first year of junior high school, and 13% in the first year of high school.

Many of patients with WPW syndrome remain asymptomatic, and outpatient management strategies are likely to vary among healthcare facilities. We inform the patients and their parents about the pathogenesis of

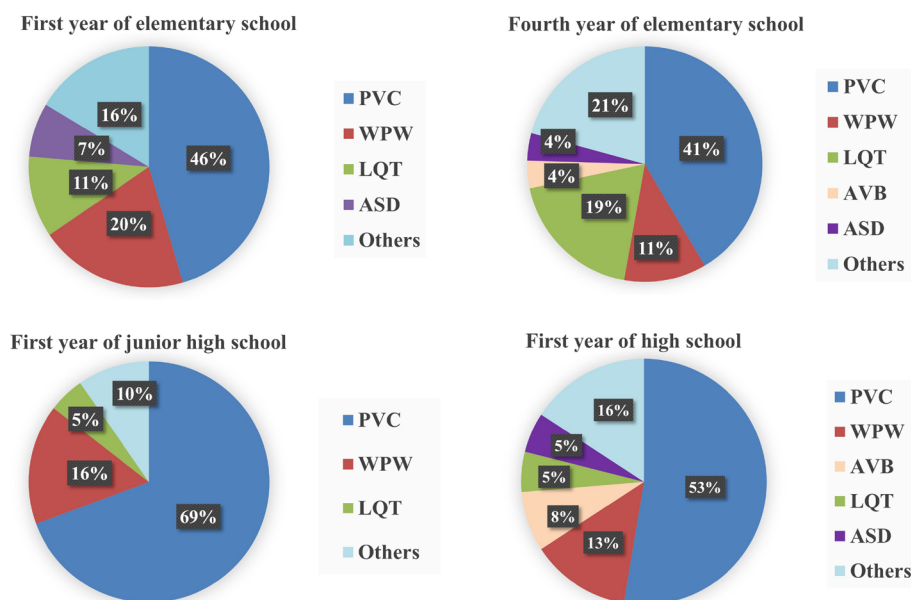


Fig. 4 Proportions of diseases diagnosed in schoolchildren who underwent school electrocardiogram screening and were referred for management to Fukui Cardiovascular Hospital from 2012 to 2020. Of the 1,754 patients, 346 (19.7%) were deemed to require observation.

ASD, atrial septal defect; AVB, atrioventricular block; LQT, long QT syndrome; PVC, premature ventricular contraction; WPW, Wolff-Parkinson-White syndrome

WPW syndrome and the probable symptoms at the first visit. Then, we instruct them to seek medical attention once symptom occurs. ECG recording during tachycardic attacks is often difficult to obtain, and decisions for treatment are usually based on patient complaints. We explain to the patients and their parents how to measure their pulse. We indicate them to monitor patient's heart rate during a tachycardic episode so that the attack can be confirmed objectively. We believe that information about age when patients are most likely to experience an attack should also be provided to ensure a prompt response in case symptoms occur.

This study has some limitations that should be considered. First, this was a single-center study with a small sample size. Second, we relied solely on symptom-based interviews, which might not have been sufficient to detect tachycardia in younger patients who could not describe their symptoms. Furthermore, other causes of tachycardic attacks, such as ANS disorders, including POTS, cannot be completely ruled out. In recent years, many reports have been published on the usefulness of wearable terminal, which are becoming increasingly popular, for the observation of heart-rate waveforms. We expect that they will be incorporated into diagnosis of tachycardic attacks.²⁴⁾

Conclusion

In this study, the most common age at tachycardia onset was approximately 12 years old. Predicting the risk of tachycardic attacks was difficult from ECG waveforms alone. Although most patients with WPW syndrome detected through school-based examinations are asymptomatic for the time being, regular checkup is recommended, especially around the age when tachycardia tends to occur.

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Conflicts of Interest

The authors declare no competing interests.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Fukui Cardiovascular Center. Approval No. 2024-012.

Data Availability

The authors confirm that the data supporting the findings of this study are available within the article.

Author Contribution

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